December 5, 1966

Jack P. Strong, M.D.
Professor and Head
Department of Pathology
Louisiana State University Medical Center
1542 Tulane Avenue
New Orleans, Louisiana 70112

Dear Doctor Strong:

In accordance with your request, we sent you application forms on October 21st, and assume that we would be receiving a proposal for an animal study on the effect of smoking and/or nicotine on atherosclerosis. I should point out that we are revising our forms and that a new modified version may be available in a few weeks. We will send you copies of these, and they may reach you in time for use in outlining your proposed investigation.

We have seen advance references to the work that you have been doing in collaboration with the Southwest Research Institute on smoking by baboons. The purpose of using baboons in cardiovascular studies, as I understand it, is that these animals develop lesions that are closely analogous to the human disease. Also, since they are omnivorous, it is said that they can be fed almost any kind of experimental diet that may be of interest in relation to cardiovascular disease. On the other hand, the cost of maintaining and studying baboons rather frightens me when I consider what must be involved. Their normal life span must be quite lengthy so that long periods of observation would be necessary. Another reason for the selection of baboons, according to some reports, is that they can be taught to smoke cigarettes as humans smoke them. This fact, if it is true, suggests that their use in behavioral studies might be quite interesting. On the other hand, one great problem, even in human studies of smoking, is the difficulty of relating actual smoke dosage to any biological or hypothetical consequence of smoking.

We have been conducting smoke inhalation experiments with small animals for about ten years. The original methods were pretty crude but, little by little, the techniques have been improved so that now we feel that we know how to carry out smoke inhalation exposures under conditions closely resembling those encountered in man, with objective measurements of actual exposure to both the particulate and gas phases of the smoke. We plan to extend these studies in an effort to get good dose response measurements in terms of pulmonary pathology.

In this field there are great advantages in the use of mice since well-standardized inbred strains are available, and relatively large numbers of animals can be used for lifetime experiments. The problem of a suitable animal model for studies of atherosclerosis appears to be somewhat difficult. Mice may

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not be very satisfactory for such work. We sponsored a few studies several years ago in which rabbits and hens, fed high cholesterol diets, were used as the model. This technique was not altogether satisfactory we thought, and we have hoped that a better model might now be available for a repetition of this kind of work.

We have been told for several years that a colony of small primates was to be set up in Boston in connection with the Harvard School of Public Health's Department of Nutrition. This has now been done and several varieties of small primates are being bred in captivity and standardized strains developed. Since dietary factors are regarded as having a relation to atherosclerosis, this colony has seemed to us to be a possibly promising locale for atherogenesis studies where standardized diets could be combined with either chronic nicotine dosage or actual smoke exposure. We have not yet entered into any actual negotiations with that group, and would certainly like to know more about the background work and pilot studies that have been carried out by you and your associates.

I think it would be a very good thing if we could get together in the very near future for a leisurely discussion of the whole problem and the various ways in which it might be approached. Around the turn of the year I am planning to make a trip to Houston and probably San Antonio on other matters. Perhaps we could also have a conference in the course of that trip, and if there is work on atherosclerosis in San Antonio that I should see I might make one visit serve several purposes.

I am enclosing copies of two publications that I happened to run into recently and which may be of some interest to you.

With kind regards,

Sincerely,

Robert C. Hockett, Ph.D.
Associate Scientific Director

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encls. 1. A. S. Milton. The effect of nicotine on blood glucose levels and plasma non-esterified fatty acid levels in the intact and adrenalectomized cat. Brit. J. Pharmacol., 26/1:256-263 (1966).
2. Robert E. Carroll. The relationship of cadmium in the air to cardiovascular disease death rates. J.A.M.A., 198/3:267-269, Oct. 17, 1966.

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